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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/088,269

09/16/2002

Olli P. Kallioniemi

4239-62295

8794

36218 7590 01/22/2009
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EXAMINER

DEJONG, ERIC S

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

01/22/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/088,269

Applicant(s)

KALLIONIEMI ET AL.

Examiner

ERIC S. DEJONG

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 9-11, 13-40, 64 and 67-70 is/are pending in the application.
- 4a) Of the above claim(s) 15-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 9-11, 13, 14, 64 and 67-70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10/24/2007.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED OFFICE ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/24/2007 and 10/14/2008 has been entered.

Claims 6-8, 12, 41-63, 65, and 66 are canceled. Claims 15-40 are withdrawn from further consideration as being directed toward a non-elected Group of invention. Claims 69 and 70 are newly presented. Claims 1-5, 9-11, 13, 14, 64, and 67-70 are currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 10/24/2007 has been considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5, 9-11, 13, 14, 64, and 67-70 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. This rejection is newly applied.

The recent en banc decision regarding *Bilski v. Warsaw* (2008) set forth that a process is patent-eligible if (1) it is tied to a particular machine or apparatus or (2) it transforms a particular article into a different state or thing. Further, the recent decision in *Comiskey* (2009) confirmed the opinion set forth in *Bilski* of the prohibition pre-empting an abstract or mental process in a claim. The revised *Comiskey* decision further reiterated the president set forth in *Richman*, 563 F.2d 1026, 1030 (CCPA 1977)). (quoting *In re* wherein the court held the application unpatentable because "if a claim [as a whole] is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory."

The instant claims are drawn to a method and the related computer program product and systems for counting nucleic acid probe signals of interest in a region of a biological specimen. The instant claims are drawn to the abstract data processing of image data. The only recitation of a physical step is the collection of confocal microscopic image data for use in said abstract data processing steps. The transformation of data in the instant case does not result in any particular physical transformation nor does it produce a result that is connected to any particular article or thing. Further, the related device and system do not serve to meaningfully limit the scope of the instant claims in that the related computer program products and system claims would wholly pre-empt the abstract data processing steps described above.

Therefore, it is maintained that the instant claims are directed to non-statutory subject matter.

Claim Rejections - 35 USC § 102

The rejection of claims 1-5, 9-11, 13, 14, 64, and 67, and 68 under 35 U.S.C. 102(b) as being anticipated by Kahn et al. (Cytometry et al. (1997) Vol. 28, pages 269-279) is withdrawn in view of amendments made to the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 9-11, 13, 14, 64, and 67-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahn et al. (Cytometry et al. (1997) Vol. 28, pages 269-279) in view of Rodenacker et al. (see IDS filed 10/07/2002). This rejection is necessitated by amendments made to the instant claims.

The instant claims are drawn to a computer implemented method for counting nucleic acid probe signals in a multi-cell region of interest in a biological spectrum comprising, obtaining a plurality of successive two dimensional image slices of said region taken at different depths along a z-axis via confocal microscopy, distinguishing spatially overlapping nucleic acid probe signals, automatically counting a number of test signals from a test probe, automatically counting a number of reference probe signals, and determining a ratio of the automatically-counted test signals to the automatically counted reference signals. The instant claims a further in a prolix form in that they recite routine procedural steps for performing spot analysis from confocal microscopy data.

Kahn et al. sets for the visualization and localization of specific DNA sequences performed by fluorescence in situ hybridization (FISH) using laser scanning confocal microscopy and Factor Analysis of Biomedical Image Sequences (FAMIS) (see Kahn et al., Abstract). The methodology is disclosed as being computer-implemented as image analysis of convention 3D reconstructions of cells were obtained by means of the Image Space software (see Kahn et al., page 277, col. 1, lines 4-14). Kahn et al. sets forth obtaining both sample analysis and construction 3D image of a sample region by collecting a series of 2D of fluorescence images at different sample depths (see Kahn et al. Figures 1A-C, page 227, col. 1, line 5 through page 278, col. 1, line 18 and page 278, col. 1, line 45 through col. 2, line 5). Figure 1C of Kahn et al. sets forth that 2D fluorescence images were obtained at different confocal plants along the z-axis. Kahn et al., and further demonstrates that overlapping fluorescent signals may be distinguished from successive 2D images taken at different sample depths by use of a factor profiles $a(i)$, $b(i)$, and $c(i)$, wherein said factor profiles were derived from 2D images obtained at different sample depths. Kahn et al. further sets forth the use of two fluorescent dyes, Fast Red (FR) and Thylozine Orange (TO) as probe labels, wherein said dyes may be used simultaneously (see Kahn et al., page 269, col. 1, line 5 through page 271, col. 2, line 4). FR is disclosed as providing a high quantum yield and was relied upon by Kahn et al. to detect small amounts of DNA sequences in individual cells, which reads on the instantly claimed limitation of a test signal from a test probe. TO was relied upon to counterstain nuclei, which reads on the instantly claimed reference signals from a reference probe. Signals from both FR and TO fluorescently labeled probes are

determined from each 2D image sequence and relied upon in the FAMIS application (see Kahn et al., page 273, col. 2, line 11, through page 275, col. 1, line 14).

Kahn et al. further teaches that problems previously resulting from the superposition of fluorescein signals, autofluorescence, and propidium iodide-stained nuclei are resolved when FR and TO spectral features are taken into account by FAMIS (see Kahn et al., page 278, col. 1, lines 20-31 and page 278, col. 2, line 22 through page 279, col. 1, line 18). Kahn et al. sets forth that although TO and FR distributions cannot be distinguished in any single 2D image, FAMIS decomposition of a plurality of 2D image sequences into specific TO and FR distributions permits a multispectral analysis. FAMIS decomposition of a plurality of 2D image sequences results in the generation of factor profiles involves transforming contiguous signals, obtained from successive 2D images, into a single curve that allows for determining which of the successive 2D images contains the strongest probe/reference signal. Direct comparison of decomposed TO and FR distributions obtained from 2D images involves the determination of a ratio of TO and FR intensities, which reads on determining a ratio of counted test signals from the test probe and counted reference signals from the reference probe. Further, all comparison of TO and FR fluorescence intensity were performed without reference to either the boundaries of a cell nucleus or of a cell. Regarding image analysis and the decomposition of images, Kahn et al. sets forth that iterative algorithms are applied by FAMIS in the analysis and computation of combined 2D images into a clustered matrices, which reads on the instantly instant limitations of

automatically counting a number of test signals and automatically counting a number of reference signals.

With regard to the expressly recited limitations directed to the processing of image data acquired from confocal microscopic data, Rodenacker et al. is relied upon to demonstrate one having ordinary skill in the art would recognize the processing as set forth in the instant claim as routine and would yielding only expected results. The recent Supreme Court decision in *KSR Intl. Co. v. Teleflex Inc.* rejected the rigid approach of applying a strict TSM test as the sole basis for obviousness and that the analysis for obviousness need not seek out precise teachings directed to the specific subject matter of a claim. Further the decision set forth that the analysis can take into account the inferences and creative steps that a person of ordinary skill in the art could employ and that a person of ordinary skill in the art is also a person of ordinary creativity, not an automaton. Further, the decision set forth that a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

Therefore, it would have been obvious to one having ordinary skill in the art to apply routine data analysis of confocal microscopic data, as set forth by Rodenacker et al., in performing a computer-implemented 3D spot counting method as instantly claimed. One of ordinary skill in the art would recognize the instant claims as a combination of familiar elements and routine experimental practices that would yield only predictable and expected result already known in the art.

Response to Arguments

Applicant's arguments with respect to claims have been considered but are moot in view of the new grounds of rejection set forth above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S DeJong/
Examiner, Art Unit 1631

